METABOLIC SYNDROME AND GENERALIZED ANXIETY DISORDER AMONG YOUNG ADULT GHANAIANS

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DECLARATION

I, Roseline Agyeiwaah Baah declare that except for other people's investigations which have been duly acknowledged, this work is the result of my own original research under the supervision of Dr. Kwame Yeboah and Dr. Thomas Tagoe and that this thesis either in whole or in part has not been presented elsewhere for another degree

..... 28 - 06 - 2022

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DEDICATION

I dedicate this work to God Almighty for life and favour throughout this journey of studies and also to my children (Lordia and Lordlyn) and my husband (Mr Kofi Anim-Bortsie).

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LIST OF ABBREVIATIONS

AHA	American Heart Association
BMI	Body Mass Index BP Blood Pressure
CAD	Coronary arterial disease
CM	Centimeter
CV	Cardiovascular
CVDs	Cardiovascular Diseases
DBP	Diastolic Blood Pressure
LHDL	Decrease High-Density Lipoprotein
DM II	Diabetes mellitus type II
FBG	Fasting Blood Glucose
FFA	Free fatty acid
GAD	Generalized Anxiety Disorder
HDL	High-density lipoprotein cholesterol
IDDM	Insulin-dependent diabetes mellitus
IFG	Impaired fasting glucose
IR	Insulin resistance
LDL	Low-density Lipoprotein cholesterol
MAP	Mean Arterial Pressure
MBP	Mean Blood Pressure
MetS	Metabolic Syndrome
NCEP	National Cholesterol Education Programme--Adult Treatment Panel (NCEP-ATP III)

NHNES	National Health and Nutrition Examination Survey
PP	Pulse Pressure
SBP	Systolic Blood Pressure
SD	Standard Deviation
SPSS	Statistical Package for Social Sciences
TC	Total Cholesterol
TG	Triglyceride
VLDL	Very Low-Density Lipoprotein
WC	Waist Circumference
W.H.O	World Health Organization
WHR	Waist Hip Ratio

ABSTRACT

Background: Mental health has been associated with cardiovascular diseases (CVDs) in several studies. Negative affective disorders like generalized anxiety disorders (GAD) and depression are common in patients with CVDs. Depression and GAD can be screen in epidemiological studies using simple standardized questionnaires, GAD-7 and patient health quaestionnaire (PHQ)-9. Metabolic syndrome is the clustering of risk factors for CVDs such as obesity, insulin resistance, hyperglycaemia, hypertension and dyslipidaemia in an individual. The presence MetS is a strong predictor of future development of CVDs. The relationship between MetS and GAD has not been reported in the Ghanaian population. This study investigates MetS in young Ghanaian adults and its relationship with GAD and depression.

General Aim: The aim of this study is to investigate the association between MetS and GAD as well as depression in young adults.

Methodology: The study was a cross-sectional design involving 364 young adults, aged 20-30 years, and recruited from Jamestown in the Accra Metropolis. The gender composition of the study participants were 174 (47.8%) males and 190 (52.2%) females. The study participants were interviewed using a structured questionnaire for socio-demographic and lifestyle information. GAD-7 and PHQ-9 instruments were used to screen GAD and depression, respectively. Anthropometric indices such as body fat, visceral fat, weight, height, waist and hip circumferences were measured. Blood pressure was measured using semiautomated blood pressure monitor. 10 millilitres of venous blood was collected and

analysed for fasting plasma glucose, lipids and triglyceride. MetS was defined using the harmonized joint interim statement criteria.

Results: The overall prevalence of MetS among the participants was 27.96%, with the female participants showing a higher prevalence of metabolic syndrome as compared to their male counterparts (37.4% vs 18.4%, p<0.001). Compared to the female participants, the male participants had high current alcohol use (33.9% vs 9.5%, p<0.001) as well as high current smoking status (13.2% vs 1.6%, p<0.001). The female participants had higher levels of systolic (119±13 vs 113±11, p< 0.001), diastolic (76±10 vs 74±8 p=0.002), pulse (76±10 vs 74±8, p=0.002) and mean (91±10 vs 87±8 p<0.001) as compared to their male counterparts. The prevalence of GAD was 39.6 % in all study participants, with females having more representation in mild anxiety category and males being presented more in moderate anxiety category. MetS was independently associated with mild [odd ratio (OR)=3.16 (1.04 – 9.59), p=0.042] and moderate [OR=1.57 (1.08 – 2.68), p=0.034] in multinominal logistic regression models. No association between depression and MetS was found.

Conclusion: There is high prevalence of MetS in our study participants, with more females having MetS compared to males. GAD was also common among young adults and it is independently associated with MetS in the study population.

CHAPTER ONE

1.0 INTRODUCTION

1.1. Background

Studies have shown that there is an increasing prevalence of metabolic syndrome (MetS) in the general population (Kassi, Pervanidou, Kaltsas, & Chrousos, 2011). The prevalence of MetS has been reported to increase with age (Ofori-Asenso, Agyeman, & Laar, 2017). The criteria used for defining MetS and the population under study has contributed to a varied prevalence (Greenstone, 2008). Irrespective of the criteria used, the prevalence of MetS was undoubtedly increasing in both developed and developing countries (Wang et al., 2008). In the United States, the prevalence of MetS was 21.8% when the age was not adjusted. The age-adjusted prevalence was however noted to be 23.7% indicating the impact of age on the prevalence of MetS (Ford, Giles, & Dietz, 2002). Among the study participants, the prevalence of MetS for people aged 20-29 and those 60-69 years were 6.7% and 43.5% respectively (Ford et al., 2002). In a previous study among 839 participants in Jamaica, the prevalence of MetS was 1.2% (Ferguson et al., 2010). In Ghana, however, the prevalence of MetS was 12.4%, higher in females than male young adult participants (Yeboah et al., 2018).

In 2005, the World Health Organization (WHO) defined mental health as "a state of well-being in which the individual realizes his or her abilities, can cope with the normal stresses of life, can work productively and fruitfully, and can contribute to his or her community. Some potential psychological risk factors for cardiovascular diseases are; Negative affective disorders (depression, anxiety, distress and anger) Personality patterns (Type A behaviour pattern and Type D personality) and Social factors (socioeconomic status and social support) (Health et al., 2005). Evidence suggests that MetS can lead to chronic stress noradrenergic dysregulation as well as endothelial dysfunction (Pan et al., 2019) which may lead to

psychiatric disorders such as generalized anxiety disorders and depression (negative affective disorder),. Generalized anxiety disorders (GAD) have been known to be one of the commonest mental disorders that are frequently encountered in primary health care. GAD is a psychiatric illness characterized by excessive worry, usually without a specific cause, for a period of at least half a year (Hou et al., 2019; Pan et al., 2019). Patients with GAD are characterized by excessive tension and uncontrollable worry about many things which affects their daily life activities. GAD is a public health concern since it affects the general population although children and middle-aged individuals have been noted to be of high risk (Mitchell, 2018). The prevalence of GAD has been variable. In a previous study, the prevalence of GAD was reported to be between 2.8% and 8.5%. The lifetime prevalence (Merikangas et al., 2010) was also reported to range from 1.5% to 3.0% in adolescents about a decade ago.

The metabolic disturbance in MetS patients may significantly contribute to brain dysfunction and consequently lead to the development of other mental disorders such as depression (Remus, Stewart, Camp, Novak, & Johnson, 2015) as well as GAD. People with GAD are often reported to have a poor health-related quality of life, frequent hospital admissions and other comorbidities such as depression, which may lead to socio-economic burden (Hinz et al., 2017). GAD has also been linked with extreme distress and severe functional impairment which could lead to economic burden as a result of decreased productivity and hospitalization (Toghanian, DiBonaventura, Järbrink, & Locklear, 2014).

1.2 Problem statement

MetS is associated with an increased risk of developing GAD and vice versa. Until recently, evidence linking anxiety to cardiovascular risk was limited to the demonstration of elevated

mortality rates among psychiatric patients with anxiety disorders (Coryell, Noyes, & Clancy, 1982). Increasing evidence now links anxiety to cardiac events in the general population (Rozanski, Blumenthal, & Kaplan, 1999). Additionally, anxiety seems to predict a greater risk of major adverse cardiac events in patients with stable CAD and to negatively influence the development and prognosis of CAD through hyper-activation of the autonomic nervous system (Lichtman et al., 2008). In a study that was conducted among Nigerian (Alebiosu & Odusan, 2004) and Zimbabwean (Isezuo & Ezunu, 2005) type 2 DM patients using the WHO definition of MetS reported a prevalence of 25.2% and 59.1% respectively. Similarly, MetS was shown to be prevalent in Ghanaians with CVDs (Alebiosu & Odusan, 2004). Nonetheless, these studies were conducted in patient populations and the underlying disease concealed the real burden of MetS (Alebiosu & Odusan, 2004) (Isezuo & Ezunu, 2005). The real weight of MetS is mainly not known in young Ghanaian adults. Also, the Cardiovascular Health Study (CHS) associated MetS with a 38% increased risk of coronary/cerebrovascular events (Sutton-Tyrrell et al., 2005). GAD on the other hand is a psychiatric illness characterized by excessive worry, usually without a specific cause, for at least six (6) months (Segal, 2010). Untreated GAD causes extreme distress, severe functional impairment when the autonomic nervous system is affected. (Rickels & Rynn, 2001) significant economic costs (Stein & Heimberg, 2004), and also elevated suicide risk (Cougle, Keough, Riccardi, & Sachs-Ericsson, 2009; Hawgood & De Leo, 2008). Effective screening strategies that will be put in place in communities and in a primary care setting where GAD is usually not thought of, would help in early detection, increase the availability of treatment interventions and consequently contribute towards improved patient outcomes (Culpepper, 2002): (Roberge et al., 2015): (Katon & Roy-Byrne, 2007). As stated earlier in previous studies untreated GAD is said to cause severe functional impairment (Rickels & Rynn, 2001) which is likely to bring about most of the components of MetS such as elevated systolic pressure, high levels of

reduced HDL, high triglyceride levels, elevated glucose levels and large waist circumference and or obesity. Excessive worry and anxious behaviours which are also characteristics of GAD are predictive of metabolic risk which may result in these affected individuals not paying attention to their eating habits, medical needs and even activities of daily living in MetS as stated early on (Hinz et al., 2017). In other studies GAD and MetS have been said to have bidirectional effects; thus either GAD leading to worsening of MetS as explained earlier or MetS leading to the worsening of GAD when one begins to worry excessively and becomes anxious when diagnosed as having MetS.

1.3. Significance

Previous studies have shown that using simple and standardized questionnaire can effectively screen GAD and depression in Ghanaian population. The reliability and validity, as well as psychosocial predictors of GAD-7 and PHQ-9 instruments for screening GAD has been reported in adolescents attending high school in Ghana (Adjorlolo, Anum, & Amin, 2020; Ahulu, Gyasi-Gyamerah, & Anum, 2020). The prevalence of GAD in antepartum and post-partum women was reported to be 11.4% and 5.4% respectively (Barthel et al., 2016). However, no study, from my literature search has reported the prevalence of GAD and depression, as well as their association with cardiometabolic risk factors in Ghana. This study would serve as a baseline data for future studies.

in the United States, the prevalence of GAD and depression was reported to be 18.1% and a 6.7% among adults (Grant et al., 2016; Kessler, Chiu, Demler, & Walters, 2005). Based on this high prevalence, of psychiatric disorders and its association with cardio-metabolic risks, it is imperative to conduct research investigations to elucidate further the physiological mechanisms underlying these conditions. Knowledge in specific mechanisms underlying

mental disorders and cardio-metabolic disease would affect health management policies leading to improved screening, diagnoses, and treatments of cardio-metabolic diseases. This is highlighted by Chapman and colleagues who stated that, "Research examining the association between depressive disorders and chronic disease suggests that timely diagnosis and treatment of psychiatric disorders could greatly affect the impact of chronic disease. The presence of mental illness may be an important contributor to the aetiology of chronic disease. Thus, the promotion of mental health would likely result in reducing a considerable proportion of the burden of chronic disease." (Chapman, Perry, & Strine, 2005).

Further understanding of the relations between these conditions (MetS, GAD, and depression) may also help control the cost of healthcare in the United States, where about 75% of healthcare finances are spent on chronic diseases. The Centers for Disease Control and Prevention (CDC), reported that $313.8 billion and $116 billion were respectively spent on both cardiovascular disease and stroke in 2009 and diabetes in 2007. This is in contrast to the costs of depression and anxiety, which average $210.5 billion and $42 billion per year respectively. Therefore, if a connection between anxiety and metabolic syndrome can be established, then early identification and treatment could prevent the development of chronic metabolic conditions and reduce the potential of healthcare cost by billions of dollars (and trillions of cedis) (Greenberg, Fournier, Sisitsky, Pike, & Kessler, 2015) when this research is conducted. The outcome of this study may also serve as baseline data for future research investigating the connection between mental disorders and chronic diseases in sub-Saharan Africans.

Finally, a unique element of this current study is that it examines metabolic syndrome components (MetS) in relation to generalized anxiety disorder (GAD) in young adults, as

previous studies have looked at obesity, anxiety and depression in children, to our knowledge, the specific associations between elevated metabolic syndrome components, anxiety and depression symptoms have not been examined (Anderson, Cohen, Naumova, Jacques, & Must, 2007; Weiss et al., 2004). It is important to establish and understand the mechanism between these conditions early in young adults, as it can lead to earlier screening, identification and intervention.

1.4. Aim and objectives

Aim

To investigate the association between metabolic syndrome (MetS) and generalized anxiety disorder (GAD).

Objectives

1. To compare the prevalence of MetS among male and female young Ghanaian adults.
2. To compare the prevalence of GAD and depression among young Ghanaian adults.
3. To investigate the association between MetS, GAD and depression among young Ghanaian adults.

CHAPTER TWO

2.0. LITERATURE REVIEW

2.1. Metabolic syndrome

Metabolic syndrome (MetS) has been defined in various ways by different organisations and this include it being the clustering of or interconnected factors that directly increase the risk of coronary heart disease (CHD), other forms of cardiovascular atherosclerotic diseases (CVD), and diabetes mellitus type 2 (T2DM)((Kassi et al., 2011). MetS has been shown to predict adverse health outcomes differentially in men and women (Stern, Williams, González-Villalpando, Hunt, & Haffner, 2004).

2.1.1 Pathophysiology of MetS

Insulin resistance is presumed to be central in the development of MetS and may be identified as the underlying process from which other abnormalities evolve (Ford, 2002). This resistance to insulin causes unhindered lipolysis leading to high delivery of free fatty acids to the liver for triglyceride synthesis and packaging into very-low-density lipoprotein (vLDL) particles (Brown & Ford, 2002). Higher vLDL levels contribute to lower HDL levels because of the reciprocal exchanges between these lipoproteins mediated by cholesterol ester transfer protein (Ford, 2002).

It has been shown further that, increase in blood pressure is related to insulin resistance sovereign of differences in age, gender and degree of obesity (Arner, 2003; Ferrannini et al., 1997; Zavaroni et al., 1992). Insulin can stimulate endothelium-dependent vasodilation and this is moderated in insulin-resistant individuals, providing a possible mechanism to explain the elevation of blood pressure in MetS. The principal evidence indicating insulin resistance as the underlying factor in MetS is also provided by the fact that pharmacologic treatment with insulin sensitizers (such as thiazolidinediones) can have advantageous effects not only

on glucose and lipids but also on blood pressure and the inflammatory and pro-atherogenic derangements previously occurring (Arner, 2003; Ferrannini et al., 1997). Visceral obesity has been suggested as the key determinant of insulin resistance and represents the major pathophysiological change leading to MetS (Wajchenberg, Giannella-Neto, Da Silva, & Santos, 2002). Adipocyte-derived humoral factors that are released in proportion to visceral fat stores facilitate effects on insulin sensitivity including free fatty acids (FFAs), TNFα, IL-6 and resistin (Tripathy et al., 2003); (Kahn & Flier, 2000). FFA is strongly supported as an inducer of insulin resistance in muscles and liver (Kahn & Flier, 2000).

The role of leptin in insulin resistance is unclear (Kahn & Flier, 2000). Whereas some studies suggest that leptin may impair insulin action, leptin therapy dramatically improves insulin sensitivity in patients with lipodystrophy (Motojima et al., 2003). Insulin resistance occurs in lean individuals, maybe due to inherited insulin receptor and post-receptor defects (Hunter & Garvey, 1998).

In biological terms, the association between MS and increased cardiovascular risk seems to be mediated by the endocannabinoid system (ECS). The mechanism of actions is through binding of endocannabinoids at the cannabinoid receptors (CB1), which then regulate appetite and energy homeostasis, emotions such as anxiety and fear, and behaviours such as food and water intake (Loh & Kew, 2008). CB1 receptors are also found in peripheral tissues such as liver, pancreas, skeletal muscle and adipose tissues, where they play an important role in lipid and glucose metabolism.

Overactivation of the ECS has been associated with metabolic alterations such as insulin resistance, dyslipidemia, lipogenesis, excessive weight gain and increasing intra-abdominal obesity (Loh & Kew, 2008). Recent data suggest that, in the presence of abdominal obesity and/or diabetes, the ECS is over activated and this contributes to further disturbances of energy balance and metabolism. In addition to regulating the intake of nutrients through

central mechanisms located within the hypothalamus and limbic area, the ECS also mediates in transport, metabolism and deposition of nutrients in the digestive tract, liver, adipose tissue, skeletal muscle and possibly the pancreas. Thus, activation of both central and peripheral CB1 receptors promotes weight gain and associated metabolic changes (Scheen & Paquot, 2009) Despite the vast number of publications devoted to MetS, the pathophysiological mechanisms' underlying it is still uncertain (Eckel, Alberti, Grundy, & Zimmet, 2010).

The pathogenesis of MetS is believed to be likely heterogeneous with obesity, psychological factors, sedentary lifestyle, unhealthy diet and largely unknown genetic factors acting together (Eckel et al., 2010). Studies have shown that MetS generally begins due to excess visceral obesity (Flegal, Carroll, Ogden, & Johnson, 2002) which results in insulin resistance which explains most of the syndrome.

The prevalence of MetS in some Asian and European countries respectively has been estimated as 9.8% and 26.2% with almost 24% of North American Adults meeting the diagnostic criteria for MetS (Aatola et al., 2010). From an analysis of data from the National Health and Nutrition Examination Survey (NHANES) III on thousands of men and women aged 20 to 70 years, (Flegal et al., 2002) showed that 24% of the adults in the United States of America (USA) had MetS, with the prevalence rising from 6.7 % among 20-29-year-old to 43.5 % among 60-69-year-old subjects (Ford, Giles, & Mokdad, 2004). The prevalence of MetS among American adults did not differ significantly among the sexes (23.7 % in women and 24% in men) (Ford et al., 2002).

Majority of epidemiological studies however have demonstrated that the prevalence of MetS is higher in men as compared to women (Marshall, Biddle, Gorely, Cameron, & Murdey,

2004). Among the ethnic groups in the USA, the Hispanics (32% of the population) were found to be the ones with the highest prevalence of MetS as compared to whites (22 %) and African-Americans (22 %) (Ford et al., 2004). The prevalence of MetS in healthy young adults in Ghana remains unknown.

According to (Grundy, 2008) about one-fourth of the European adult population can by the various MetS definition be said to have the condition. In line with the U.S.A data, the prevalence of MetS varies in Europe by age group and characteristics of the population studied, geographic location and criteria used. Early on in Finland, the prevalence of MetS in the FINRISK cohort (aged 45 to 64 years) was significantly higher in men than in women (39 % vs. 22 %) (McNeill et al., 2005). The prevalence tended to increase with age and associated with abnormalities in glucose metabolism (McNeill et al., 2005). In a study at Botnia ((Isomaa et al., 2001). MetS were diagnosed in 10 % of women and 15 % of men with normal glucose tolerance, 42 % and 64 % of those with increased fasting glucose or impaired glucose tolerance, and 78 % and 84% of those with DM II.

2.1.2 Diagnosis and risk factors of metabolic syndrome

The concept of 'syndrome X', (which he later renamed MetS) was first put forward by Reaven, making a hypothesis that, it was a central feature in the development of CHD and DMT2, mainly through target tissue resistance to insulin action. From that time, many international organizations and expert groups, such as the World Health Organization (WHO), the European Group for the study of Insulin Resistance (EGIR), the National Cholesterol Education Program Adult Treatment Panel III (NCEP: ATPIII), American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI), and the American Association of Clinical Endocrinology (AACE), the International Diabetes Federation (IDF), have tried to incorporate all the varying parameters used to define MetS.

WHO made the first approach in 1998, which proposed that the presence of impaired glucose tolerance (IGT) or DMT2, an important or essential component of the syndrome, together with at least two of the following parameters: raised BP, hypertriglyceridemia and/or low HDL-cholesterol, obesity (as measured by waist/hip ratio or body mass index (BMI)), and micro-albuminuria (K. G. M. M. Alberti & Zimmet, 1998). The EGIR excluded micro-albuminuria as an integral component of the syndrome shortly thereafter, while it required hyper-insulinemia to be present (Borch-Johnsen et al., 1999). Waist circumference and not BMI was accepted as the main indicator to assess obesity while introducing different cut-offs from those previously used for the other components of the syndrome.

In 2001, the NCEP-ATP III published a new set of criteria that included waist circumference, blood lipids, BP, and fasting glucose. The NCEP-ATP III definition differed from both the WHO and EGIR definitions in that, IR was not considered as a necessary diagnostic component. MetS may be defined by the current diagnostic standard provided by NCEP-ATP III, as a constitution of clinical characteristics associated with an increase in the risk of DM II and CVDs (NCEP/ATP, 2001). (Haffner, 2006) defined MetS as a collection of metabolic abnormalities associated with insulin resistance that predisposes affected individuals to atherosclerosis and consequently increased risk of cardiovascular (CV) events. The main components of metabolic syndrome are dyslipidemia (elevated triglycerides and apolipoprotein B (apo B)-containing lipoproteins, and low high-density lipoproteins (HDL), the elevation of arterial blood pressure (BP) and deregulated glucose homeostasis, while abdominal obesity and/or insulin resistance (IR) have gained increasing attention as the core manifestations of the Syndrome. Metabolic syndrome is said to be one of the most formidable challenges in contemporary public health ((Kaur, 2014). MetS is associated with three of the six leading causes of death worldwide: cardiovascular disease, stroke, and diabetes (Organization, 2017). It is said that, individuals with metabolic syndrome are five (5) times

more likely to develop type 2 diabetes, two(2) times more at risk to develop cardiovascular disease within 5 to 10 years of being diagnosed with metabolic syndrome, and 2 to 4 times more likely to suffer a stroke (K. Alberti et al., 2009). In the United States, from 2003 to 2012, the overall prevalence of the syndrome was 33%, with women having significantly higher rates (35.6%) than males (30.3%) Additionally, age is a risk factor for metabolic syndrome, with a prevalence of 50% in adults over the age of 60 (Aguilar, Bhuket, Torres, Liu, & Wong, 2015).

Metabolic syndrome as defined in relation to the updated definition of the American Heart Association and the National Heart, Lung and Blood Institutes. National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP III) according to Grundy 2005, requires the presence of three or more of the following five criteria:

- **HDL**: < 40 mg/dL (0.9 mmol/L) for men, < 50 mg/dL (1.1 mmol/L) for women;
- **Fasting triglycerides**: ≥ 150 mg/dL (1.7 mmol/L) or relevant drug treatment;
- **Fasting hyperglycemia**: ≥ 6.1mmol/l (100 mg/dL) or on drug therapy for elevated glucose (NCEP, 2001).
- **Blood pressure:** systolic blood pressure ≥ 130 mmHg and/or diastolic ≥ 85 mmHg or on antihypertensive medication;
- **Abdominal obesity**: waist circumference ≥102cm (40inches) for men and 88cm (35inches) for women.

    - The NCEP ATP-III blood pressure criterion is considered as MetS if the value is above the cut-off *or* the subject is taking anti-hypertensive medication;
    - The NCEP ATP-III HDL cholesterol criterion is considered as MetS if the value is below the cut-off.

- The triglyceride criterion is considered MetS if the subject is above the cut-off *or* taking relevant medication.

HDL ("good cholesterol") functions by carrying low-density lipoproteins ("bad cholesterol") to the liver, which then removes them. High levels of low-density lipoproteins are related to artery hardening, which results in impeded blood flow.

As a result, high levels of low-density lipoprotein have negative metabolic effects, whereas high levels HDL promote good metabolic effect (Park et al., 2015); (Hippe et al., 2018).

Triglycerides are a measure of the amount of lipids in the blood. Unused calories are stored and provide the body with energy when there is low blood glucose between meals. High levels of triglycerides play a role in thickening and hardening of arterial walls, and this is known as atherosclerosis and are linked to the increased risks of stroke and cardiovascular disease (Nishimura et al., 2017); (Martin et al., 2015).

Fasting glucose or hyperglycemia is a measure of the amount of glucose in the blood after at least eight hours of fasting. Glucose, a simple sugar which is derived from food is used to generate energy for the body's cells. Glucose on entering the bloodstream through the intestines after ingestion of food cause a rise or high levels of sugar in the blood, so after fasting, if levels are high it indicates that the body is not utilizing insulin properly for transporting glucose into cells. This may predict the presence of diabetes or a pre-diabetic state and over time, can also lead to problems such as heart attacks and strokes (Sonne & Hemmingsen, 2017).

Systolic blood pressure on the other hand is the pressure in the arteries during cardiac muscle contraction (ventricular systole). High systolic blood pressure may result from several factors (such as unhealthy lifestyle, medications, and stress-induced vasoconstriction (artery

narrowing) among other reasons and it is also a known risk factor of cardiovascular disease and stroke (Michael, 2017).

Finally, a high BMI, abdominal or central obesity is an indication of large quantities of visceral body fat, and this can be considered as a possible cause of metabolic syndrome independent of waist circumference. In clinical practice and research, BMI can serve as a simple tool to indicate or predict body fat and metabolic risk (Janssen, Heymsfield, Allison, Kotler, & Ross, 2002).

2.1.3 Genetic basis of Mets

In defining the precise genetic abnormalities related to MetS, a lot of effort has been put into it (Dorresteijn et al., 2012). Several candidate genes have been proposed that include genes regulating peroxisome proliferator-activated receptor γ (PPAR-γ), leptin, adiponectin, glucocorticoids and lipoprotein lipase (Esposito et al., 2003). Several studies have attempted to identify primary genetic risk factors but no study has yet been able to identify genetic variants common to more than two of the components (Sumner et al., 2010). Reports from the Malmö Preventive Project, a large prospective study of 16,143 non-diabetic individuals showed that polymorphisms in susceptibility genes for DM II (TCF7L2, WFS1, and IGF2BP2) and obesity (FTO) predispose to MetS by increasing the risk of one or two specific components of MetS. However, the outcomes argue against a common genetic background of MetS (Zeggini et al., 2008).

2.1.4 Lifestyle effect on MetS

An inactive lifestyle is associated with several features of MetS (insulin resistance, dyslipidemia, hypertension, obesity, elevation in ROS species etc) (Lakka et al., 2002).

Individuals with low levels of leisure-time physical activity and cardio-respiratory fitness are more likely to have MetS (Lakka et al., 2002). In contrast, individuals with physically active life may prevent the onset of MetS (Hunt, Resendez, Williams, Haffner, & Stern, 2004). A randomized controlled trials data indicate that exercise training has at least modest effects on individual features of the MetS, there is still some uncertainty whether exercise training can prevent or treat the MetS itself (Lakka et al., 2002).

In a population-based study of 612 middle-aged Finnish men who were involved in moderate-or high-intensity leisure-time physical activity for at least 3 hours/week were half as likely as sedentary men to develop MetS during the 4-year follow-up period (Lakka et al., 2002). From the Diabetes Prevention Study conducted, results showed that counselling of middle-aged, overweight participants to reduce weight and increase physical activity, reduced the amassed incidence of diabetes over 4 years by 58 % compared with a control group (Timpson et al., 2009). Additionally, increased participation in moderate-to-vigorous aerobic physical activity and regular long-term participation in resistance training improved MetS status among adults with impaired glucose tolerance (Herder et al.,2009).

Long term physical activity, even in the absence of weight loss, may prevent MetS (IlanneParikka et al., 2004). Weight shedding is valuable for treating all of the components of MetS including obesity, hypertension, dyslipidemia hyperglycemia and insulin resistance (Grundy, 2008). The Finnish Diabetes Prevention Study disclosed that lifestyle intervention reduced the occurrence of abdominal obesity and the overall prevalence of MetS in the long term (Herder et al., 2009). Even a modest weight loss as 5-10 % of body weight can significantly reduce triglycerides and increase HDL (Eckel et al., 2010).

According to a recent study, dairy intake was contrariwise associated with the prevalence of MetS in seven out of 13 studies, suggesting that dairy consumption may have a positive effect

on MetS (Crichton, Bryan, Buckley, & Murphy, 2011). Again a large Finnish population-based cohort study of middle-aged subjects disclosed that increased daily sodium intake was an independent dietary indicator of MetS in middle-aged subjects. The seafoods that are moderately lower in carbohydrate (45 %), and moderately higher in fat (35-40 %), with less than 10 % of saturated fat, may be advantageous for improving features of MetS, including effects on insulin sensitivity, serum lipids and liver function.(Vanhatalo et al., 2010).

The link between alcohol intake and MetS remains contentious (Lee et al., 2010). In some cross-sectional studies, moderate alcohol consumption has been related to a lower prevalence of MetS (Freiberg et al., 2004). A population-based study of clinically healthy men showed that there was no difference in alcohol intake across the groups of men with none of the components of the MetS (Carr et al., 2004). On the order hand, a large Korean study showed an increasing dose-response relation between alcohol consumption and MetS (Yoon et al., 2006) and in another study, there was an autonomous relation between insulin sensitivity, as measured by the clamp technique, and alcohol intake (Balkau et al., 2007).

Smoking is known to be a strong risk factor for atherosclerosis and CVD and it may also have a dose-dependent association with MetS (Dorresteijn et al., 2012).

2.2 Generalized anxiety disorder (GAD)

Generalized anxiety disorder (GAD) is characterized by persistent anxiety and worry and is the most common anxiety disorder with reported prevalence rates ranging between 2.8% and 8.5% (Roy-Byrne *et al*, 2004; Stein,2004). GAD causes extreme distress, severe functional impairment if not managed or treated (Andrews *et al* 2010) significant economic costs (Stein, 2004), and is independently associated with elevated suicide risk (Hawgood, 2008; Cougle, 2009). Generalized anxiety disorder (GAD) diagnosis since its introduction into DSM-III (American Psychiatric Association, 1980), has lots of controversies surrounding it. Precedent

to this time, GAD was conceptualized as one of the two main components of Anxiety Neurosis, the other being panic (American Psychiatric Association, 1968). On recognition that GAD and panic were often time, occurring together and sufficiently different to be considered independent disorders, led to their separation in DSM-III: where a diagnosis of GAD required uncontrollable and diffuse anxiety or worry that was excessive or unrealistic, in relation to objective life circumstances that persisted for one month or longer in addition to several psychophysiological symptoms.

Generalize anxiety disorder (GAD) is one of the most common anxiety disorders witnessed in general medical practice and the general population. This disorder has an estimated current prevalence of 2.8% to 8.5% in the general population of 1.6% to 5.0% in general medical practice (Olfons *et al* 1997; Roy-Byrne *et al* 2004; Leon *et al* 1995).

According to Breslau *et al* (1985), it was noted that, in samples taken for an earlier clinical study using DSM-III, GAD hardly occurred without major depression (MD) and this resulted in a suggestion that GAD will be conceptualized as a residual, or severity marker of major depression (MD) (Brown *et al.*, 1998, Cloninger *et al.*, 1990, Offord *et al.*, 1994).

2.2.1 Pathophysiology of GAD

2.2.1.1 Psychological Theories

Psychological theories form the basis of several therapeutic approaches. Common interventions including cognitive behavioral therapy (CBT), relaxation therapy, stimulus control, cognitive restructuring, and self-monitoring are based on these theories. Medications are usually not the remedy for anxiety disorders as they oppress activity in the amygdala and other areas of the brain that underlie the disorder (Stahl 2013). Where fear and anxiety are

known responses in GAD, medications will not change this neuronal learning. So to control anxiety, some form of psychological therapy will be required. However, there is a suggestion of combining these two treatments. The data confirming the superiority of this combination therapy approach over monotherapy are lacking. Differentiating fear and anxiety is difficult since they are usually co-occurring and share most of their characteristics. One helpful way to theorize them is to think of fear as a response to an immediate threat, whereas anxiety is usually an anticipatory response to perceived or real future events (APA 2013). Worry is the cognitive reaction to fear and anxiety. Worry entails negative mental images and emotions. Although some might think of worry as a cause of anxiety, worry appears to be an attempt at self-protection from the more tragic consequences of the feared object (Behar 2009). The individual may deceptively interpret worry as an effective coping mechanism. Worry, however, becomes pathologic when it is excessive and is a core feature of GAD.

Acquiring fears is a normal part of development. Fears can develop in a typical conditioning paradigm. Aversive happenings in life can be viewed as undefined stimuli. When paired with a neutral stimulus, these eventually become a conditioned stimulus that can stimulate fear (CR). Under normal circumstances, this process is adaptive because it helps the patient avoid potentially harmful things. If other neutral stimuli become feared (conditioned stimulus and CR), the person's fears become more general. This paradigm involves circuits in the amygdala, hypothalamus, and prefrontal cortex. Investigators have proposed that patients with anxiety have exaggerated responses to danger cues and a reduced response to safety cues that would ease the fear response (Lissek 2005). Serotonin appears to be involved in controlling responsiveness to threatening cues. One study found that citalopram decreased amygdala responses to threat presentations, suggesting this as one way that selective

serotonin reuptake inhibitors (SSRIs) affect anxiety (Harmer 2006). Because fear acquisition is a learning process, psychologic approaches such as CBT may also affect fear conditioning.

2.2.1.2. Neurobiological Theories

The area of the brain where fear conditioning is concentrated is the amygdala. Sensory input is received from areas of the brain such as the sensory thalamus, sensory cortex, and prefrontal cortex. Connections between the amygdala and areas of the prefrontal cortex regulate the experience of fear and the resulting psychological responses. Motor responses may be controlled by connections with the periaqueductal region of the brain. When this system is not regulated appropriately a clinical anxiety syndrome may result. Similarly, worry, a cognitive process, may be controlled by cortico-striato-thalamo-cortical circuitry (CSTC). These paths involve neurotransmitters and receptors that may be targeted for pharmacotherapy. Several neurotransmitter paths in the amygdala and CSTC are involved in fear, anxiety, and worry (Stahl 2013; Stein 2009; Kim 2005). An important inhibitory neurotransmitter in the brain is ϒ-Aminobutyric acid (GABA). For anxiety, the GABA receptor appears most pertinent. This receptor complex involves five subunits and a central channel through which Chloride ions enter into the cell when an agonist such as GABA binds to it. These subunits have been designated α, β, ϒ, and δ. The inflow of chloride reduces neuronal electrical activity and thus is inhibitory. Ligands such as benzodiazepines bind and act as allosteric modulators. The GABA receptor subtypes where benzodiazepines appear to exert anxiolytic properties have two β subunits plus either ϒ2 or ϒ3 plus two from the α1, α2, or α3 types. In the presence of GABA, benzodiazepines appear to further augment inhibition and reduce anxiety and fear responses in the amygdala and worry in the CSTC. Serotonin is an important neurotransmitter in both the amygdala and the prefrontal cortex. Neuronal projections involving serotonin from the dorsal raphe nucleus to the amygdala and frontal

cortex are thought to be involved in anticipatory anxiety and avoidance, which is conditioned fear (Nutt, 2001). Overactivity of the serotonin system may be involved in anxiety disorders (Connor & Davidson, 1998)Activation of presynaptic serotonin-1 receptors leads to an initial decrease in serotonin activity, followed by an increase. It is thought that the action of buspirone at these receptors explains its activity. The delayed action of buspirone may suggest that long-term neuronal adaptation is responsible for its therapeutic benefit, rather than the acute increase in serotonin function (M Stahl, Lee-Zimmerman, Cartwright, & Ann Morrissette, 2013). Serotonergic drugs are effective for depression, which has several symptoms that overlap with GAD. Patients with both depression and anxiety treated with SSRIs not only had improvements in depressive symptoms but also improvements in anxiety, which led to trials of SSRIs and serotonin-norepinephrine reuptake inhibitors (SNRIs) for anxiety disorders, which are indeed effective for GAD. The initial increase in serotonin activity can cause anxiety symptoms, but with time, there is neuronal and receptor adaptation and more normal output from the amygdala and the CSTC (Stahl, 2013). The exact mechanism for the initial increase in serotonin activity, which is unclear, may involve more than one neurotransmitter action. Stimulation of postsynaptic serotonin-2 receptors in the limbic system may also lead to avoidance and anxiety (Conner 1998). Blocking these receptors can be beneficial. Quetiapine, which may act as a serotonin-1 partial agonist and serotonin-2 antagonist, is beneficial for anxiety (Sheehan 2013).

Another important receptor type is the voltage-sensitive calcium channel (VSCC). This receptor is similar to the GABA receptor because it is made up of several subunits. These are found in both the amygdala and the prefrontal cortex. Overactivity of this receptor in the amygdala is thought to result in the fear/anxiety response and worry in the CSTC (Stahl

2013). The VSCC that includes the α2δ subunit appears to be the target for both pregabalin and gabapentin, both of which reduce anxiety.

2.3 MetS and GAD

Anxiety is said to triggers activation of the human stress system through behavioural and physiological changes that improve the ability of the organism to regulate homeostasis and increase its chances for survival. Adversely, these processes appear to affect autonomic and hormonal regulation, resulting in metabolic abnormalities, inflammation, insulin resistance and endothelial dysfunction (Das and O'keefe, 2008). The most accepted underlying mechanism relies on the hypothesis that increased activation of the HPA axis could be pathophysiologically involved in the concomitant occurrence of the typical MetS risk factors and stress**.** Results from earlier studies on the association between metabolic syndrome and GAD are controversial. Concerning anxiety disorders, several studies have identified metabolic associations. For instance, a study looking at Vietnam War veterans discovered that a diagnosis of generalized anxiety disorder positively associated with metabolic syndrome, whereas depression was not (Carroll *et al.,* 2009).

Similarly, another study by Luppino and colleagues (2011) found a strong association between most metabolic syndrome components and anxiety-specific affects, but not depression-specific affects. By contrast, however, other recent studies have found that the prevalence of metabolic syndrome was greater only in individuals with depression, but not anxiety (Butnoriene, Bunevicius, Norkus, & Bunevicius, 2014). Another study found that as levels of depression increased, the number of components of metabolic syndrome exhibited also increased, even when controlling for obesity, smoking status, socioeconomic status, age, lifestyle, and comorbidity with anxiety. This relationship was not observed with anxiety

symptoms (Skilton, Moulin, Terra, & Bonnet, 2007). However, as the duration of GAD increased, this comorbidity weakened (Breslau & Davis, 1985b), leading the GAD duration requirement to be increased to six months in DSM-III-R (American Psychiatric Association, 1987) and DSM-IV (American Psychiatric Association, 1994). Generalized Anxiety Disorder (GAD) is usually assessed by the use of the GAD-7 scale.

2.4 MetS and depression

In a review and meta-analysis examining the link between depression and MetS reported a positive and bidirectional association (Pan et al, 2012). Lifetime history of major depression was also found to predict the development of MetS in middle-aged women (Goldbacher et al 2009). Moreover, disturbance to biological rhythms (sleep, social, activities, and eating pattern) has been associated with key components of MetS in community adults with major depressive disorder (Moreira *et a*l, 2016) and bipolar disorder (BD), while a recent meta-analysis demonstrated a higher risk of MetS in subjects with BD than the general population, with a prevalence of approximately 30% (Czepielewski, Daruy Filho, Brietzke, & Grassi-Oliveira, 2013). In a subsequent study, it was found that MetS and its components were associated with increased suicide risk, signifying that public mental health interventions targeting suicide reduction may need to focus on individuals with MetS and its components (Czepielewski et al., 2013). Taken together, these studies have shown that patients with psychiatric disorders have a high mortality risk, mainly for cardiovascular events, which could be Correspondence up to three times higher than that of the general population. By contrast, however, other recent studies have found that the prevalence of metabolic syndrome was greater only in individuals with depression, but not anxiety (Butnoriene, Bunevicius, Norkus, & Bunevicius, 2014). Another study found that as levels of depression increased, the number of components of metabolic syndrome exhibited also increased, even when

controlling for obesity, smoking status, socioeconomic status, age, lifestyle, and comorbidity with anxiety. This relationship was not observed with anxiety symptoms (Skilton, Moulin, Terra, & Bonnet, 2007). Other studies have found no association between depression or anxiety and metabolic problems. For example, a study in Finland found that after sex, alcohol consumption, smoking, marital status, education level, and physical activity were controlled for, metabolic syndrome was not associated with anxiety or depression in young adults (Herva et al., 2006). Affirming these findings, a large longitudinal study conducted in Norway found no association between anxiety and depression and future metabolic syndrome (Hildrum, Mykletun, Midthjell, Ismail, & Dahl, 2009)

CHAPTER THREE

3.0. METHODOLOGY

3.1 Study design

A population-based cross-sectional design was used. The study subjects were apparently healthy male and female young Ghanaian adults within the age brackets of twenty to thirty years.

3.2 Study setting

The study was conducted at Jamestown in Accra, Ghana. Accra is the capital and largest city of Ghana; with an estimated urban population of 3.27 million as of 2012. The actual respondents were selected from Jamestown a suburb of Accra. Jamestown is located east of the Korle lagoon. It is one of the oldest settlements in the city of Accra and emerged as a community around the 17th century British James Fort on the Gulf of Guinea coast. It is an area of a dense mixture of commercial and residential facilities. Jamestown remains a fishing community inhabited primarily by the indigenes of the Ga tribe. Although in a state of decay following years of neglect by subsequent governments, the community is a popular tourist destination for those seeking to see the remnants of Accra's colonial past.

3.3 Study population

The study participants were apparently healthy young adults within the ages of twenty and thirty years. The study participants did not have any history of cardiovascular, respiratory, renal, psychiatric and endocrine diseases.

3.4 Eligibility criteria

3.4.1 Inclusion criteria:

Participants were recruited if the following criteria were met:

- An adult between 20-30 years of age and of sound mind to provide voluntary informed consent.
- Ghanaian ethnic background.
- Those that are not mourning from the loss of a relative for the past three months.

3.4.2 Exclusion criteria:

Participants were excluded from the study based on the following:

- Subjects outside the age range were not included.
- Pregnant adults and lactating mothers
- Self-reported history of any endocrine, renal and cardiovascular disorders.
- Those with known psychiatric conditions
- Those that are mourning.

3.5 Sample size determination

The sample size for this study was calculated from the formula (Cochran, 1963) below:

$$n = \frac{Z^2 \times p \times q}{E^2}$$

Where n is the sample size; Z is the coefficient of significance (1.96) for significance level (q) of 5% (0.05) and E being the allowable error margin of 16%. Thus, substituting these parameters in the formula above, the sample size, n was 300. Thus, 364 subjects were recruited for the study.

3.6 Recruitment of study subjects

A convenient sampling technique was used to recruit the study participants who responded favourably to the invitation to participate in the study. An advertisement was done Jamestown, Accra and given those who responded were scheduled for specified dates on which they would take part in the study. Before the data collection, participants were educated on the fasting guidelines; overnight fasting between 8–12 hours before blood samples were taken. The objectives of the study, the procedure involved and possible risk and benefits were thoroughly explained to each participant. The potential participants were asked to sign/ thumbprint a consent form (Appendix C). The participants were transported on the morning of their scheduled dates to the Department of Physiology to take part in the study after meeting the fasting requirement. All the measurements were done between 6 am to 9 am at the human laboratory of the Department of Physiology. The samples of blood were analyzed at the Medicaid Diagnostics and Laboratory, Koforidua.

3.7 Questionnaire administration

Structured Questionnaires (Appendix B) was used to collect the data from the study participants. The questionnaire contained questions which assessed: socio-demographic and lifestyle information and this helped to assess the respondents' CVDs risk. Information on the questionnaire was explained to the study participants.

3.8 Anthropometry

Weight was measured with participants barefooted and wearing light clothing using the Omron digital scale (HN-288), and was recorded to the nearest 0.1kg. Height was measured using the Seca Stadiometer (Seca, Germany) with subjects in a standing position and without shoes, with shoulders in normal alignment. Body mass index (BMI in kg/m^2) was calculated

for each participant as the individual's body weight (in kilograms) divided by the square of height (in meters). BMI was categorized as underweight (BMI < 18.50 kg/m2), normal weight (BMI: 18.50 – 24.99 kg/m2), overweight (BMI: 25.00 – 29.99 kg/m2) and obese (BMI ≥ 30 kg/m2).

In the measurement of waist and hip circumference, each participant was made to stand with his arms at the sides, feet positioned close together, and weight evenly distributed across the feet. Measurements for waist circumference were made at the end of a normal expiration, with a non-elastic tape measure, at the approximate midpoint between the lower margin of the last palpable rib and the top of the iliac crest. Hip circumference was measured at the level of the greater trochanters. The waist-hip ratio was determined as the ratio of waist circumference and the circumference of the hips.

3.9 Body composition

The body composition was measured using the Omron Body Composition Monitor (BF- 506, Omron Healthcare, Inc., Vernon Hills, IL, USA). The measurements were performed in a standing position, with electrodes in contact with soles and heels of both feet. Biological impedance was measured with 4 terminals. The participant‘s age, gender and height were entered into the equipment and the participant was asked to stand upright (straight torso) on the platform in the same condition as the weight measurement. The participant then grabbed the grip of the electrodes of the monitor by placing the palm around the electrodes while placing the thumbs up, resting on the top of the unit, and stretches the arms forward to approximately 90o to the axis of the body. The body fat percentage (%), visceral fat level and BMI in kg m^{-2} were computed for each patient. This device sends a non-detectable low electrical current of 50 kHz and500mA through the body to determine the amount of fat tissue. Muscles, blood vessels and bones are body tissues with large water content, thus they

conduct the electrical current with less resistance. Body fat has a lower electrical conductivity. The proportion of fat in the body is calculated using five variables: electric resistance, height, weight, age and sex.

3.10 Blood pressure measurements of participants

Systolic and diastolic blood pressures were measured using an automated digital blood pressure monitor (Omron 991 XL, Healthcare, Inc., Vernon Hills, IL). Before blood pressure (BP) measurement, the participants were asked to empty their urinary bladder if they have not passed out urine within the last four (4) hours. The blood pressure cuff was placed on the left arm of the participant lying in a supine position; with the lower edge of the cuff about 2-3 cm above the elbow crease and the bladder centred over the brachial artery. The arm was rested on a table and raised so that the cuff was at level with the heart. The subject was allowed to rest for at least 5 minutes. The blood pressure was measured three times; each measurement was spaced with at least 60 seconds interval with the preceding measurement. The first measurement was discarded and the last two measurements were averaged to give the true blood pressure.

3.11. Definition of metabolic syndrome (JIS)

The most widely accepted definition currently was proposed by Alberti *et al.*, in the Joint Interim Statement. This document proposes that the presence of three of the following criteria are needed for a diagnosis of MS: elevated waist circumference (according to population and country-specific definitions) triglycerides 150 mg/dl or greater; high-density lipoprotein (HDL)-cholesterol lower than 40mg/dl in men and 50mg/dl in women. Blood pressure of 130/85mmHg or greater and fasting glucose 10mg/dl or greater. This definition highlights

that there should be no obligatory component for MS but rather all individual components should be considered on cardiovascular risk prediction (Alberti et al,2009).

3.12 Generalized anxiety disorder assessment (GAD-7 SCALE)

- The GAD-7 is a self-administered patient questionnaire normally used as a screening tool for generalized anxiety disorder and, also to measure the severity in patients already diagnosed with GAD. It has a unidimensional structure matching the original structure of Diagnostic Statistical Manual of Mental Disorders, Fourth Edition Text Revision diagnostic criteria with all items measuring the same concept and in the same direction. It is composed of seven (7) items corresponding to symptoms based on the criteria for GAD in the DSM Manual of Mental Disorders including:
    - feeling nervous, anxious or on edge,
    - not being able to stop or control worrying,
    - worrying too much about different things,
    - trouble relaxing,
    - being so restless that it is hard to sit still,
    - becoming easily annoyed or irritable, and
    - feeling afraid as if something awful might happen.

The period that is used in GAD-7 is the two previous weeks and, through a 4-point Likert scale from 'not at all' to 'nearly every day', the patient is asked how often he/she had been bothered by any of the presented problems. The GAD-7 index is obtained by adding the scores from the questionnaire, after having assigned 0 to the least severe situation, 3 to the most severe one, and 1 and 2 to the intermediate ones. The cut-off points 5, 10 and 15 allow us to classify the anxiety as none/normal (0–4), mild (5–9), moderate (10–14), and severe

(15–21). In general, anyone who scores 8 or above can be considered as having significant anxiety symptoms (Sousa et al., 2015).

3.13 Patient Depression Questionnaire (PHQ-9)

The PHQ-9 was developed to make a critical based diagnosis of major depressive disorder the PHQ-9 comprises nine items that evaluate the presence of nine Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition Text Revision (American Psychiatric Association, 2000a) criteria for major depressive disorder in the previous 2 weeks. Each item of the PHQ-9 is rated on a 4-point scale ranging from 0 (not at all) to 3 (nearly every day), for a total score of ranging from 0-27. A higher score indicated an increased severity of symptoms and an increased likelihood of major depressive disorder. Questionnaires with up to two missing values are scored, replacing any missing values with the average score of the completed items (Kroenke, 2001). Cutoffs of 5, 10,15 and 20 represent mild, moderate and moderately severe and severe levels of depressive symptoms, respectively (Korenke et al, 2010).

3.14 Biochemistry and clinical analysis

3.14.1 Blood sample collection

After 8-12 hours of overnight fast, 10 millilitres (10mls) of venous blood samples were collected from the antecubital area. The 10mls was divided into 2mls for fluoride (ash top) tubes for fasting plasma glucose (FPG) measurement, 5mls into EDTA (violet top) tubes and 3mls into gel-separator tubes (yellow top). The tubes were centrifuged at 3000 rpm for 10 minutes to obtain clear plasma and sera. Plasma glucose was measured enzymatically within 15 minutes after sample collection. Plasma and serum samples were aliquoted into sterile Eppendorf tubes and stored at -20°C until further analysis.

3.14.2 Chemical principle – glucose oxidase test for fasting plasma glucose

The level of glucose in the fasting plasma glucose was measured with a Selectra Junior chemical auto analyzer from the United Kingdom (Bayer Diagnostics, UK), using ELITech glucose PAP SL reagent from ELITech clinical systems, France, following the manufacturer's instructions. The analysis involves enzymatic oxidation of glucose to form an equimolar amount of gluconic acid and hydrogen peroxide.

Glucose + O2 + H2O ⟶ GOD ⟶ gluconic acid + H_2O_2

The hydrogen peroxide formed reacts, under the catalysis of peroxidase, with phenol and 4-aminophenazone to form a red-violet quinoneimine dye as an indicator.

2H2O2 +4-aminophenazone +phenol ⟶ POD ⟶ quinoneimine + 4 H2O

The concentration was determined by the equipment after reading the absorbance of the indicator at a wavelength of 500 nm.

3.14.3 Plasma lipid profile assay

Lipid profile of plasma was analyzed using Selectra Junior chemical auto analyzer from the United Kingdom (Bayer Diagnostics, UK), using ELITech cholesterol SL, ELITech cholesterol HDL SL 2G and ELITech triglycerides Mono SL New reagents from ELITech clinical systems, France, following the manufacturer's instructions.

The total amount of cholesterol (TChol) in the plasma was assayed after enzymatic hydrolysis and oxidation. Briefly, cholesterol ester in the plasma was hydrolyzed by cholesterol esterase to form cholesterol and fatty acids.

Cholesterol ester + H2O ⟶ cholesterol ester ⟶ cholesterol + fatty acids

The cholesterol was oxidized afterwards, by cholesterol oxidase to form cholestene-3-one and hydrogen peroxide.

Cholesterol + O2 ⟶ cholesterol oxidase ⟶ cholestene-3-one + H2O2

Plasma triglycerides (TG) were assayed after enzymatic hydrolysis with lipases. Triglycerides are hydrolyzed by lipases to form glycerol and fatty acids.

Triglycerides + H2O $\longrightarrow$ lipases $\longrightarrow$ glycerol + fatty acids

Phosphate is transferred from adenosine triphosphate (ATP) to glycerol, under the catalysis of glycerolkinase (GK), to form glycerol-3-phosphate, which is oxidized by glycerol-3-phosphate oxidase (GPO) to form dihydroacetonephosphate and hydrogen peroxide.

Glycerol + ATP $\longrightarrow$ GK $\longrightarrow$ glycerol-3-phosphate +ADP

Glycerol-3-phosphate + O_2 $\longrightarrow$ GPO $\longrightarrow$ dihydroacetonephosphate + H_2O_2

The hydrogen peroxide formed reacts, under the catalysis of peroxidase, with phenol and 4-aminophenazone to form a red-violet quinoneimine dye as an indicator.

$2H_2O_2$ +4-aminophenazone +phenol $\longrightarrow$ POD $\longrightarrow$ quinoneimine + 4 H_2O

The concentration was determined by the equipment after reading the absorbance of the indicator at a wavelength of 500 nm.

HDL cholesterol was assayed by the precipitation method. 500 µL of the diluted precipitant solution, containing phosphotungstic acid in the presence of magnesium, was added to 200 µL of the plasma sample. The sample was allowed to sit for 10 minutes at room temperature and centrifuged afterwards at 4000g for 10 minutes to precipitate low-density lipoproteins and chylomicrons. The HDL cholesterol was assayed from the supernatant solution at an absorbance of 500nm. The levels of LDL cholesterol were calculated from Frieldwald's equation, LDL = TChol – (HDL+TG/2.2).

3.15 Data handling

Codes were assigned to individual participants. The data was entered into an Excel spreadsheet, cleaned and exported into SPSS database. Adequate file security was put in

place to ensure confidentiality. The hard copies of the questionnaire and participants test results were kept secured and confidential.

3.16 Data analysis

The data was analyzed using Statistical Package for Social Sciences (SPSS) software, version 20. The data with continuous variables were tested for normality using Shapiro-Wilk test and variables with normal distribution were presented as mean± standard deviation, whereas non-normal distribution variables were presented as median (interquartile range). Independent Student's t-test was used to analyze the means of data with two predictors. Categorical data were presented as frequency (percentage) and analyzed by Chi-square ($\chi 2$) test when necessary. Association between variables was analyzed using Pearson's correlation for normally distributed data and Spearman's correlation for non-normally distributed data. A 95% confidence interval was used and considered a value of $p < 0.05$ as statistically significant.

3.17 Ethical Approval

Ethical approval was granted by the Ethics and Protocol Review Committee of the College of Health Sciences, University of Ghana (Protocol ID number: CHS-Et/M.8-P.3/2016-2017). The study was conducted in conformity with the Helsinki Declaration on Human Experimentation, 1964 with subsequent revisions, latest Seoul, October 2008 (Williams, 2008). Only participants meeting the eligibility criteria were recruited for the study. All study participants were adequately informed of the purpose, nature, procedures, risks and hazards of the study. A written informed consent (Appendix C) was obtained from all the participants who were included in the study.

CHAPTER FOUR

4.0 DESCRIPTION OF RESULTS

4.1 Clinical and Anthropometric characteristics of study participants.

A total of 364 participants who were young adults and between the ages of 20-30, made up of 174 (47.8%) males and 190 (52.2%) females were studied. Based on gender, no difference in their age was observed. Compared to female participants, male participants had higher current and former smoke and alcohol intake. Males participants were taller, had higher waist circumference, waist-to- Hip and visceral fat ratio than the females. Female participants on the other hand had higher BMI, hip circumference and body fat as compared to their male participant (Table 1).

Table 1 Clinical and Anthropometric characteristics of study participants

Parameters	Male (n=174)	Female (n=190)	p
Age (years)	25±2.8	24.8±3.1	0.569
Smoking status, n (%)			
Current	23 (13.2)	3 (1.6)	<0.001
Former	32 (18.4)	7 (3.7)	0.03
Never	119 (68.4)	180 (94.7)	0.74
Alcohol status, n (%)			
Current	59 (33.9)	18 (9.5)	<0.001
Former	67 (38.5)	20 (10.5)	0.03
Never	48 (27.6)	152 (80)	<0.001
Weight, Kg	68.1±8.9	70.1±10.7	0.56
Height, cm	168.3±7.5	165.6±6.3	< 0.001
BMI, kgm-2	24.1±3.3	25.6±4.1	<0.001
Waist circumference, cm	89±16	86±17	0.067
Hip circumference, cm	96±15	100±16	0.025
Waist-hip ratio	0.95±0.2	0.88±0.18	0.602
Visceral fat, %	5.3±3.5	4.6±0.9	0.115
Body fat, %	25.2±7.6	28.1±9.3	<0.001

BMI; Body mass index. Data are presented as mean (± standard deviation). p values were determined using t-tests.

4.2 Biochemistry parameters of study participants

Female participants had higher fasting plasma glucose as compared to their male counterparts. The mean levels of triglycerides, LDL cholesterol and vLDL cholesterol were similar between male and female participants (Table 2).

Table 2. Biochemistry parameters of study participants.

Parameters	Male	Female	P
Fasting Plasma Glucose, mmol/l	4.6±1.0	5.2±1.3	<0.001
Triglyceride, mmol/l	1.5±0.4	1.6±0.4	0.082
Total cholesterol, mmol/l	5.2±1.2	5.1±1.0	0.389
HDL cholesterol, mmol/l	1.1±0.4	1.1±0.6	0.880
LDL cholesterol, mmol/l	3.6±1.3	3.6±1.3	0.763
vLDL cholesterol, mmol/l	0.34±0.1	0.36±0.2	0.815

HDL: High-Density Lipoprotein; LDL: Low-Density Lipoprotein; vLDL: Very Low-Density Lipoprotein; Data are presented as mean (± standard deviation) p values were determined using t-test

4.3 Hemodynamic parameters of study participants.

Females had significantly higher mean SBP and DBP among the study subjects ($p<0.001$ and 0.002 respectively). The pulse BP and mean BP were also significantly higher in the female subjects ($p<0.001$) (Table 4.3).

Table 3. Hemodynamic parameters of study participants.

Parameters	Male	Female	P
Systolic BP, mmHg	113±11	119±13	< 0.001
Diastolic BP, mmHg	74±8	76±10	0.002
Pulse BP, mmHg	74±8	76±10	0.002
Mean BP, mmHg	87±8	91±10	<0.001

BP; Blood pressure; Data are presented as mean (± standard deviation), p values were determined using t-tests.

4.4 Prevalence of obesity and metabolic syndrome

The prevalence of obesity in the components of MetS among the study participants are shown in Figure 1. Female participants had higher levels of obesity compared to male participants ($\chi^2=15.34$, $p=0.002$).

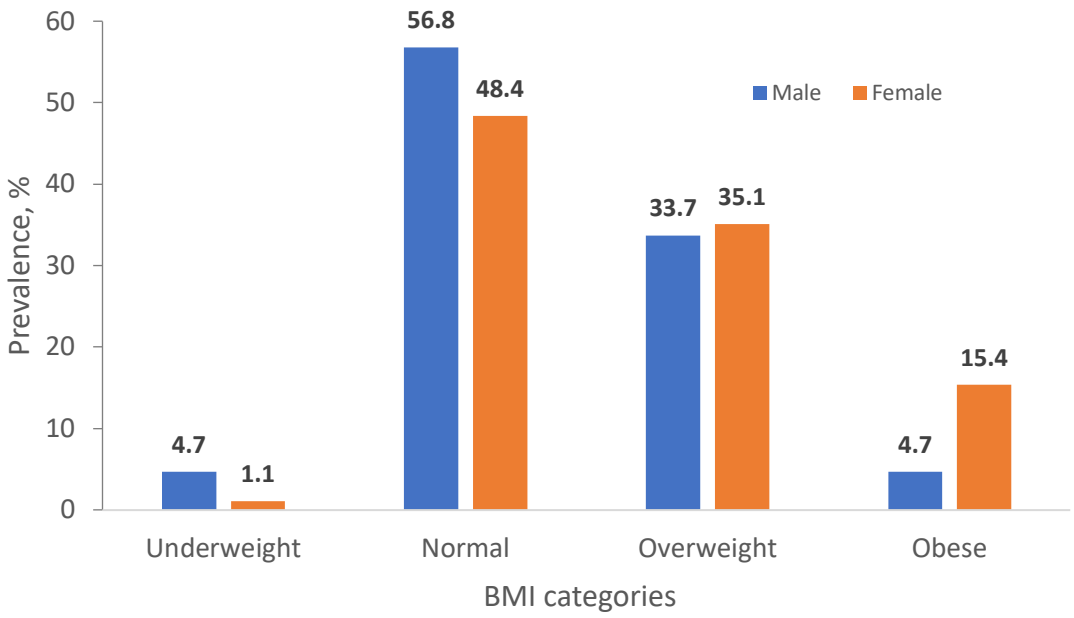

Figure 1 BMI categories of study participants by gender

4.5 Number of components of metabolic syndrome by gender.

The number of components of metabolic syndrome by gender is shown in Figure 2 below. There were higher proportions of female participants with a high number of components of metabolic syndrome compared to male participants (χ^2=36.75, p<0.001).

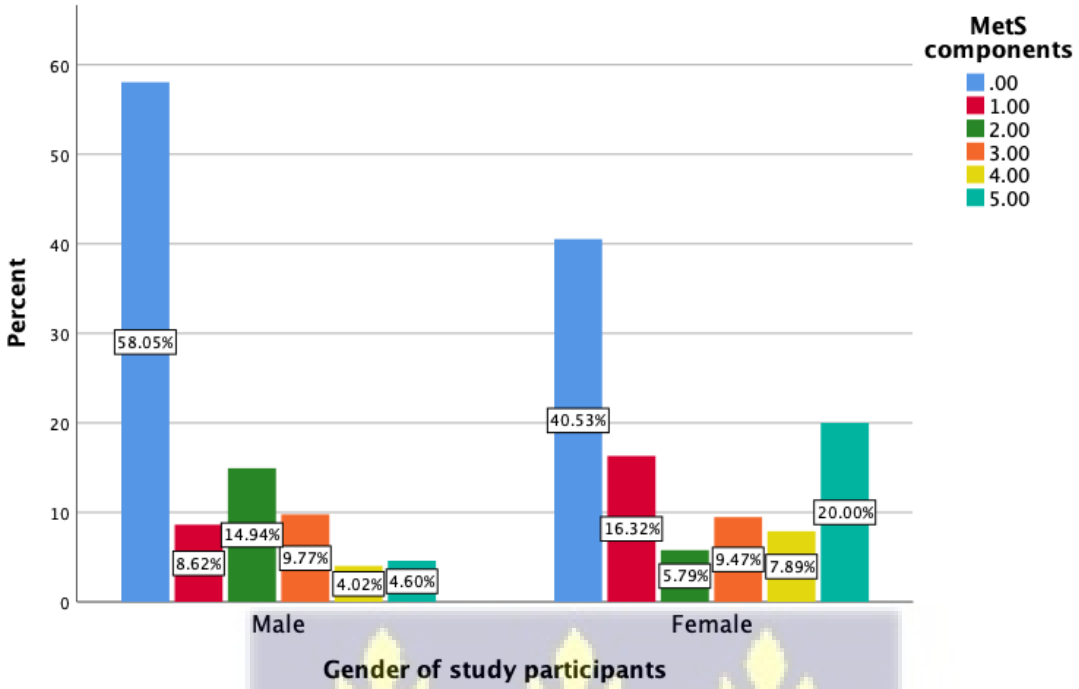

Figure 2 Number of components of metabolic syndrome by gender

4.6 Prevalence of metabolic syndrome by gender

The prevalence of metabolic syndrome by gender is shown in Figure 3 below. Compared to male participants, female participants had a higher proportion of metabolic syndrome (χ^2=16.12, p<0.001).

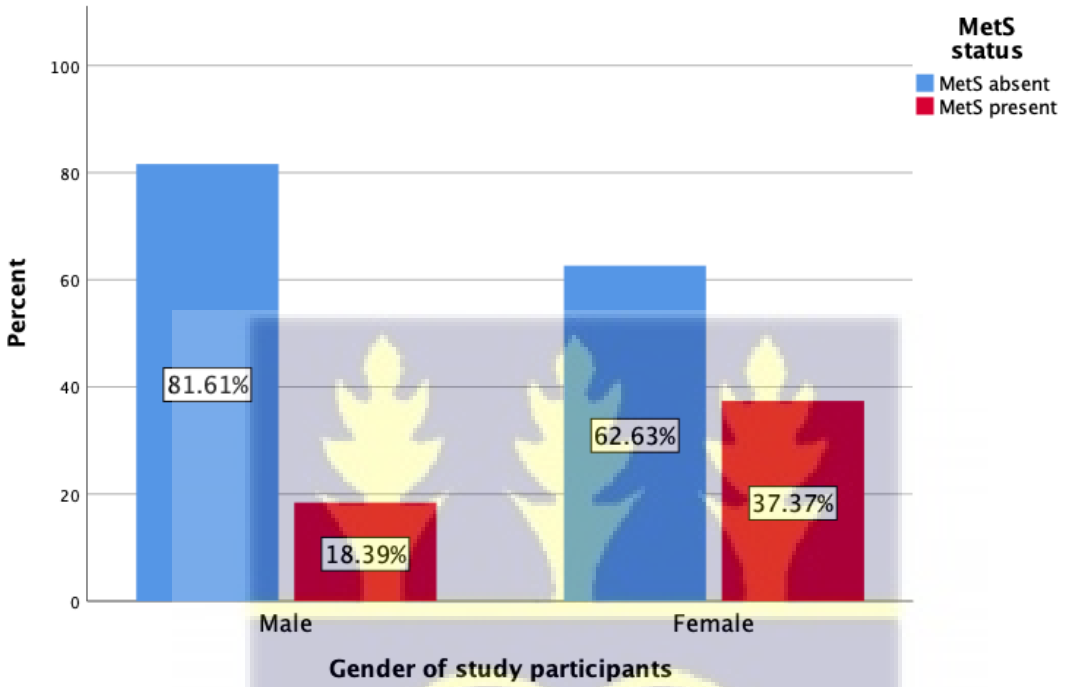

Figure 3 Prevalence of metabolic syndrome by gender

4.7 Prevalence of Generalized Anxiety Disorder (GAD)

The prevalence of GAD among study participants is shown in Figure 4 below. Females, as compared to males, had a high prevalence in the Mild Anxiety levels category while males had a higher prevalence in moderate anxiety.

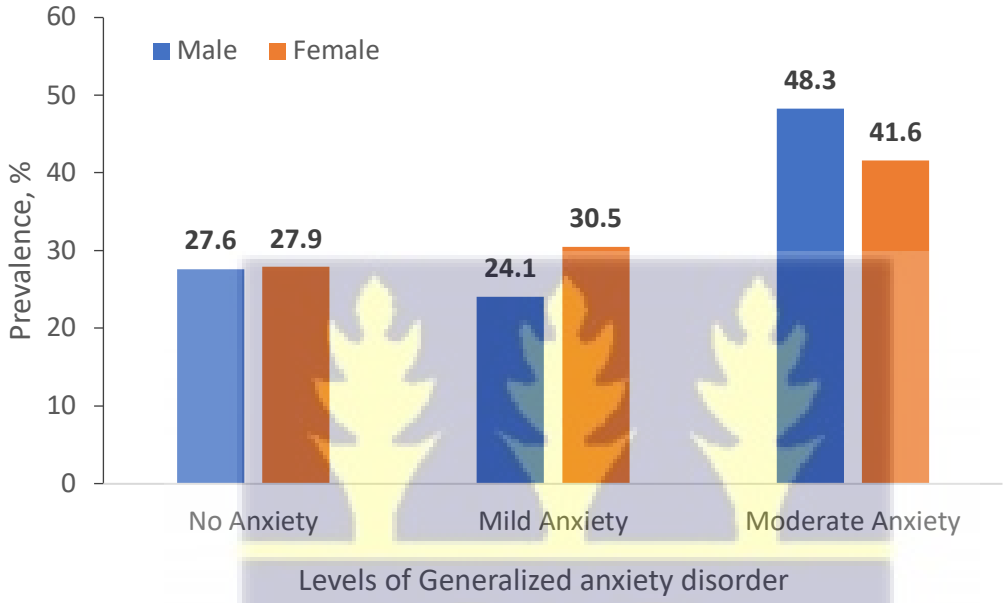

Figure 4 Levels of generalized anxiety disorder by gender

4.8 Prevalence of depression

From Figure 3 it is observed that females tend to have a high prevalence of depression in the minimal and severe depression categories with males having high prevalence only in the mild/moderate depression category. However, these differences were not statistically significant ($p > 0.05$).

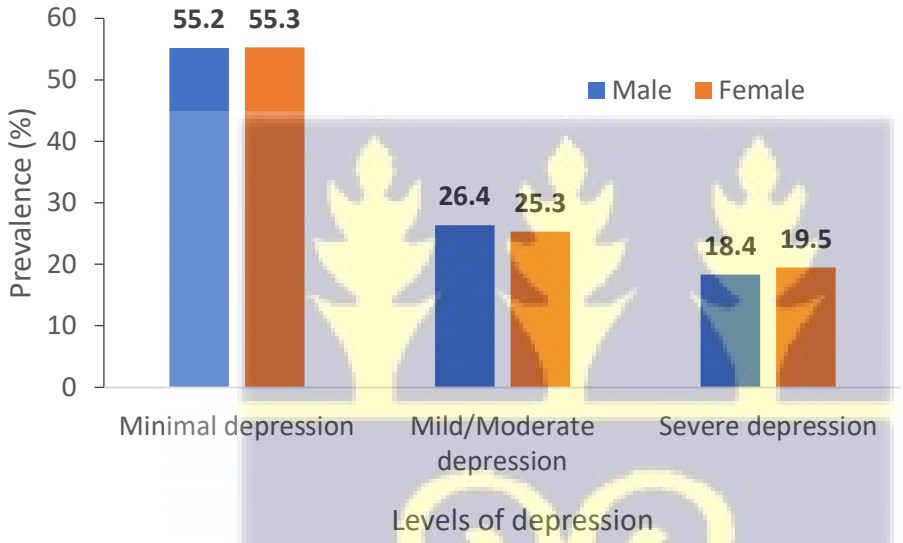

Figure 5 Levels of depression by gender

4.9 Components of metabolic syndrome and its relation to GAD.

More females had hyperglycemia compared to their male counterparts across the GAD levels (p=0.001, <0.001 and 0.064 for no anxiety, mild anxiety and moderate anxiety respectively). Among the females who had hyperglycemia, a greater proportion was observed in the mild anxiety category. The proportion of females with high BP was also noted to be higher than the males with high BP across the GAD category. Of this, the prevalence of high BP was 32.8% in the mild anxiety group, higher than the other two groups (no anxiety and moderate anxiety). The prevalence of females with high WC was high in the moderate anxiety group (43.0%) whereas more females were observed as having hypertriglyceridemia in the mild anxiety category. When comparing the prevalence of low HDL, it was observed that more females had low HDL, which was higher in those with mild anxiety (Table 4.4).

4.10 Components of MetS and its relation to GAD and Obesity

The prevalence of obese with no anxiety was significantly higher compared to non-obese who also had no anxiety (p<0.001). Among the GAD category, it was noted that 83.3% of obese with moderate anxiety had hyperglycemia. More so obese (100%) had high BP in the no anxiety category compared to the other GAD groups. The prevalence of obese with high WC, hypertriglyceridemia and low LDL was higher in the obese group across the GAD categories (p-value = 0.006, <0.001 and <0.001 for no anxiety, mild anxiety and moderate anxiety respectively) (Table 4.5).

Table 4 Components of metabolic syndrome and its relation to GAD.

	No anxiety			Mild anxiety			Moderate anxiety		
	Male	**Female**	**P**	**Male**	**Female**	**P**	**male**	**Female**	**P**
Hyperglycemia mmol/l	2 (4.2)	11 (20.8)	0.001	1 (2.4)	17(29.3)	<0.001	10 (11.9)	18 (22.8)	0.064
High BP mmHg	5 (10.4)	15(28.3)	0.021	6 (14.3)	19(32.8)	0.031	15(17.9)	22 (27.8)	0.127
High WC (cm)	7(14.6)	20 (37.7)	0.008	9 (21.4)	21(36.2)	0.107	17 (20.2)	34 (43)	0.002
Hypertriglyceridemia	13(27.1)	22(41.5)	0.126	13 (31)	27(46.6)	0.114	33 (39.3)	32 (40.5)	0.874
Low HDL(mmol/l)	16(33.3)	25 (47.2)	0.156	12 (28.6)	33(56.9)	0.004	29 (34.5)	41 (51.9)	0.025

BP: Blood pressure; WC: Waist Circumference; HDL: High-Density Lipoprotein; Data are presented as mean (± standard deviation) p values were determined using t-test

Table 5: Components of MetS and its relation to GAD and Obesity.

	No anxiety			Mild anxiety			Moderate anxiety		
	Non-obese	obese	P	Non-obese	Obese	p	Non-obese	Obese	p
Hyperglycemia mmol/l	10 (10.3)	3 (75)	<0.001	6(7.1)	12 (80)	<0.001	13 (9)	15 (83.3)	<0.001
High BP mmHg	16 (16.5)	4 (100)	<0.001	12 (14.1)	13(86.7)	<0.001	21 (14.5)	16 (88.9)	<0.001
High WC(cm)	23 (23.7)	4 (100)	0.001	15 (17.6)	15 (100)	<0.001	33 (22.8)	18 (100)	<0.001
Hypertriglyceridemia	31 (32)	4 (100)	0.003	25 (29.4)	15 (100)	<0.001	47 (32.4)	18 (100)	<0.001
Low HDL(mmol/l)	37 (38.1)	4 (100)	0.006	30 (35.3)	15 (100)	<0.001	52 (35.9)	18 (100)	<0.001

BP: Blood pressure; WC: Waist Circumference; HDL: High-Density Lipoprotein; Data are presented as mean (± standard deviation)

p values were determined using t-test

4.11 Components of MetS and its relation to Depression and Gender.

The proportion of females with minimal depression and hyperglycemia was observed to be higher compared to males (p=0.001). A similar trend was observed in the other two groups (mild depression and severe depression groups). Similar to the observation made from individuals with minimal depression and high BP, more females (32.9%) were also noted as having high BP in the minimal depression group. Although females generally were noted to have hypertriglyceridemia and low HDL, a greater proportion was seen in the mild/moderate depression group and severe depression group respectively (Table 4.6).

4.12 Components of MetS and its relation to Depression and Obesity.

The percentage of obese with hyperglycemia was higher in the minimal depression category. A total of 86.4% obese with hyperglycemia had minimum depression compared to 7.3% non-obese with hyperglycemia in the minimal depression category. A total of 100% obese with hyperglycemia also fell under severe depression category. Obese with hypertriglyceridemia was more than non-obese with hypertriglyceridemia in the minimal depression category. A similar trend was also observed in the other two categories (mild/moderate depression and severe depression). Subjects who were obese with low HDL were more than those without obese with low LDL in all the three categories of depression (Table 4.7).

Table 6: Components of MetS and its relation to Depression and Gender.

	Minimal depression			Mild/Moderate depression			Severe depression		
	Male	**Female**	**P**	**Male**	**Female**	**P**	**male**	**female**	**P**
Hyperglycemia mmol/l	7 (7.3)	25(23.8)	0.001	6(13)	14 (29.2)	0.053	0 (0)	7 (18.9)	0.002
High BP mmHg	15 (15.6)	34(32.4)	0.005	7(15.2)	15 (31.3)	0.066	4(12.4)	7 (18.9)	0.465
High WC (cm)	19 (19.8)	39(37.1)	0.007	11 (23.9)	24 (50)	0.009	3 (9.4)	12(32.4)	0.021
Hypertriglyceridemia	28 (29.2)	40(38.1)	0.181	21 (45.7)	25 (52.1)	0.53	10(31.3)	16(43.2)	0.305
Low HDL mmol/l	29 (30.2)	50(47.6)	0.012	20 (43.5)	27 (56.3)	0.215	8 (25)	22(59.5)	0.003

BP: Blood pressure; WC: Waist Circumference; HDL: High-Density Lipoprotein; Data are presented as mean (± standard deviation) p values were determined using t-test

Table 7: Components of MetS and its relation to Depression and Obesity.

	Minimal depression			Mild/Moderate depression			Severe depression		
	Non-obese	obese	P	Non-obese	Obese	P	Non-obese	Obese	P
Hyperglycemia mmol/l	13 (7.3)	19 (86.4)	<0.001	11 (13.4)	9 (75)	<0.001	5 (7.6)	2 (66.7)	0.001
High BP mmHg	28 (15.6)	21 (95.5)	<0.001	13 (15.9)	9 (75)	<0.001	8 (12.1)	3 (100)	0.001
High WC (cm)	36 (20.1)	22 (100)	<0.001	34 (41.5)	12 (100)	<0.001	12(18.2)	3 (100)	0.001
Hypertriglyceridemia	46 (25.7)	22 (100)	<0.001	34 (41.5)	12 (100)	<0.001	23(34.8)	3 (100)	0.014
Low HDL mmol/l	57 (31.8)	22 (100)	<0.001	35 (42.7)	12 (100)	<0.001	27(40.1)	3 (100)	0.023

BP: Blood pressure; WC: Waist Circumference; HDL: High-Density Lipoprotein; Data are presented as mean (± standard deviation) p values were determined using t-test

4.13 Association between metabolic syndrome and generalized anxiety disorder

Multinominal logistics regression models were constructed to investigate the association between metabolic syndrome and GAD and the results are shown in Table 8. Compared to participants with no GAD, participants with increased BMI and metabolic syndrome have an increased likelihood of having mild anxiety and moderate anxiety, whereas male gender decreases the likelihood of having mild anxiety and moderate anxiety.

Table 8: Determinants of generalized anxiety disorder

Parameter Estimates

Levels of GAD		OR	p
Mild Anxiety	Intercept		0.027
	Age (years)	0.96 (0.87 – 1.05	0.352
	BMI kg/m2	1.16 (1.01 – 1.33)	0.038
	Waist circumference (cm)	1.02 (0.99 – 1.05)	0.221
	Systolic BP mmHg	1.02 (0.99 – 1.06)	0.276
	MetS present	3.16 (1.04 – 9.59)	0.042
	Male gender	0.97 (0.79 – 1.09)	0.037
Moderate Anxiety	Intercept		0.015
	Age (years)	0.99 (0.9 – 1.08)	0.775
	BMI kg/m2	1.15 (1.02 – 1.3)	0.026
	Waist circumference (cm)	0.99 (0.97 – 1.02)	0.693
	Systolic BP mmHg	1.01 (0.98 – 1.04)	0.467
	MetS present	1.57 (1.08 – 2.68)	0.034
	Male gender	0.88 (0.64 – .98)	0.016

The reference category: No Anxiety. OR(odds ratio), CI (confidence interval).

4.14 Association between metabolic syndrome and depression.

Multinominal logistics regression models were constructed to investigate the association between metabolic syndrome and levels of depression and the results are shown in Table 9. However, none of the parameters included in the model was associated with levels of depression.

Table 9: Determinants of depression.

Parameter Estimates

Levels of depression		OR (95% CI)	P
Mild/Moderate depression	Intercept		0.961
	Age years	0.99 (0.92 – 1.09)	0.983
	BMI kg/m2	0.96 (0.85 – 1.08)	0.518
	Waist circumference cm	1.01 (0.98 – 1.04)	0.549
	Systolic BP mmHg	0.99 (0.96 – 1.02)	0.589
	MetS present	1.69 (0.88 – 2.74)	0.434
	Male gender	0.94 (0.53 – 1.66)	0.828
Severe depression	Intercept		0.328
	Age (years)	1.05 (0.96 – 1.16)	0.31
	BMI (kg/m2)	0.97 (0.85 – 1.11)	0.652
	Waist circumference cm	0.99 (0.97 – 1.03)	0.779
	Systolic BP mmHg	0.99 (0.97 – 1.03)	0.97
	MetS present	1.22 (0.43 – 3.48)	0.714
	Male gender	0.79 (0.42 – 1.5)	0.479

The reference category: No depression. OR (odd ratio), CI (confidence interval).

CHAPTER FIVE

DISCUSSION, CONCLUSION AND RECOMMENDATIONS

5.1 General characteristics of study participants

The findings of the study showed that the male participants had high alcohol intake compared to their female counterparts who had a low prevalence of MetS. This is in agreement with the findings of a cross-sectional study conducted in the US from the Third National Health and Nutrition Examination Survey on Alcohol consumption and the prevalence of MetS (Freiberg, Cabral, Heeren, Vasan, & Ellison, 2004). In that study, it was reported that moderate alcohol consumption is associated with a lower prevalence of MetS. In contrast to the findings of this current study, a longitudinal study (2007- 2013) on drinking behaviour and prevalence of MetS among Korean men aged between 20 to 79 years reported an increasing dose-response relationship between alcohol consumption and MetS (Yoon, Kim, Thuras, Grant, & Westermeyer, 2006). Female participants were also found to have significantly high BMIs and body fat as compared to their male counterparts (Yoon et al., 2006). This finding is inconsistent with the findings of the Czech epidemiological study, dubbed; the MONICA study, which reported that the prevalence of obesity was 24.4% in women and 32% in men aged 25–64 years, with men having higher BMIs (Pelikánová, 2003). A contrasting finding by the American Diabetes Association in a study Intra-abdominal fat is a major determinant of the NCEP III Criteria for MetS, reported that the prevalence of high body fat did not differ significantly between sexes (24.0 % in men and 23.7 % in women) (Carr et al., 2004).

5.2 Hemodynamic parameters of study participants

The study results depicted a significant difference in the blood pressures (BP) of males and females. Female, as compared to their male counterparts, had high blood pressures. The

results indicated that the female participants had significantly high values of systolic BP, diastolic BP, pulse BP and consequently mean BP as compared to their male counterparts. This study is contrary to studies that have been conducted in the past on premenopausal women and hormone regulation that helps to keep females blood pressures under control (Yanes & Reckelhoff, 2011). Thus the prevalence of hypertension is also higher in men until after menopause in women when the prevalence of hypertension becomes higher in women than age-matched men (Yanes & Reckelhoff, 2011). This also contrasts previous findings that males have higher blood pressures than females. A relationship between indices of sympathetic activity and vascular resistance across the age span was found in men (Maranon & Reckelhoff, 2013). These sex and age differences in vascular resistance are largely a result of changes in the balance of vasodilating and vasoconstricting adrenergic receptor tone. When these changes are considered along with cardiac output, a rational picture then begins to develop why blood pressure rises more with age in women than men. Differences in blood pressure regulation in relation to gender or sex are said to be likely reflected by differences in the relationships among the following variables such as sex-specific conditions, including the menstrual cycle, pregnancy, oral contraceptives and menopause, can have additional impacts on these relationships (Joyner, Wallin, & Charkoudian, 2016).

5.3 The prevalence of MetS in study participants

From the study, the results showed that the overall prevalence of MetS in the study participants was (27.96%). The findings are however a bit higher than the findings of (Alebiosu & Odusan, 2004) where the prevalence of MetS was at 25.2%. The findings are also in line with the findings of (de Ferranti et al., 2004) where the highest prevalence of MetS among USA ethnic groups was found in Hispanics to be (32 % of the population) compared to whites (22 %) and African-Americans (22 %). The study findings are however

closely consistent with the findings of studies based on the general population in Ghana that established MetS prevalence, determined with the three definition criteria as; 3.9% (NCEP ATP III), 2.2% (WHO), and 7.8% (IDF) (Titty, Owiredu, & Agyei-Frempong, 2008).

The study showed that female participants had high MetS prevalence (37.4%) as compared to the male participants (18.4%) among the study population of Ghana. This result is similar to MetS studies in different populations (Ashtari, Salari, Aminoroaya, Deljoo, & Moeini, 2012);(Cai et al., 2012) (Ashtari et al., 2012), where a higher prevalence of MetS was observed in women than in men. Also, (Berlin, Lin, Lima, & Bertoni, 2012) found that patients with MetS were more likely to be females, slightly younger and none smokers. The findings were in contrast with the findings of the Czech epidemiological study; MONICA, that discovered that MetS occurs in 24.4% of women and 32.0% of men aged 25–64 years (Pelikánová, 2003). The female participants had higher prevalence with 3 to 5 the components of MetS being present. The results indicate that among the females as compared to the males, there was a high prevalence of; hyperglycemia, low high-density lipoprotein cholesterol and high waist circumference. This finding is similar to that of (Ashtari et al., 2012) where MetS components were prevalent among males and females but slightly higher in the females.

5.4 Prevalence of generalized anxiety disorder (GAD).

The overall prevalence of GAD was observed to be 39.6%, comparable in males (19.9%) and females (19.8%). This suggests that males and females may both experience excessive anxiety and worry, occurring with associated restlessness, fatigue, difficulty concentrating, irritability, muscle tension as well as disturbed sleep. In other previous studies, GAD was noted as the common anxiety disorder with varied prevalence, ranging between 2.8% and

8.5% (Ruscio et al., 2007). The prevalence of GAD was higher than what was obtained in an earlier study (39.6% versus 22%). Findings from this study on the prevalence of GAD in relation to gender (the male and female subjects) are different from the results obtained from a previous study in the U.S, where an estimated 2.7% adults had GAD. And this was found to be higher in females (3.4%) than for males (1.9%). Results obtained from previous studies (higher prevalence of GAD in females compared to males) may be due to many factors contributing to higher rates of diagnosed anxiety in women, ranging from hormone fluctuations to brain chemistry. A high percentage (25.8%) in the prevalence of anxious women was found in Brazil (compared with 14.1% of Brazilian men) and a low rate of anxious women was found in Turkey (1.1% compared with 0.5% of anxious Turkish men) contrary to what was observed in this current study. Findings from this study suggest that anxiety disorder is not connected to gender. Therefore, both males and females may have the same chance of having GAD in the Ghanaian population.

5.5 Prevalence of Depression

In this study, it was observed that there was no significant difference in the levels of prevalence of depression among the study participants; both male (27.5%) and female (27.5%). This observed prevalence is in contrast to that of a study that was done in Mangalore, Karnataka among young adults between the ages of 18-30yrs where females were found to have a high prevalence of depression compared to males. In an earlier study conducted among an older adult population (50yrs and above) both in Ghana and in South Africa for 2 years it was discovered that the prevalence of mild depression was 6.7% and 2.7% in Ghana and South Africa, respectively ($p<.001$), with a gender difference only in Ghana. Some of the factors that were independently associated with depression among women in Ghana were lack of current work and migration. In the same way, higher age, lack

of current work and lower quality of life were also independently associated with depression among women in South Africa. In conclusion, Ghana had a higher depression rate than South Africa and different factors were identified in association with depression among men and women in these two countries (Thapa, Martinez, & Clausen, 2014).

5.6 Association between obesity and GAD

From the study, obesity was significantly associated with GAD at all the levels of anxiety and an even closer association was found at the moderate anxiety level. A study among a population of undergraduates in Nigeria had contrasting reports of no significant association or correlation between the studied variables; Obesity and GAD (Ejike, 2013). In another study where meta-analysis of data from the Rochester Epidemiology Project (REP) was done to examine associations between anxiety disorders and BMI (obese) among adults ages 18-85 living in Olmsted County, MN in 2009, it was found out that there was an inverse correlation between anxiety and obesity. In a previous study by (Gariepy, Nitka, & Schmitz, 2010), findings were consistent with findings that obesity is associated with anxiety. Obesity is theorised to be a risk factor for anxiety disorders but evidence supporting an association between these two conditions is not clear. Factors such as immuno-inflammatory processes, oxidative stress, neurotransmitter balance, neuroprogression, unhealthy dietary patterns, lower rates of physical activity and increased sedentary behaviours usually seen in obese patients may have contributed to the observed GAD (DeJesus et al., 2016).

5.7 Association between MetS and GAD

In a recent study on the association between major depressive disorder (MDD), generalized anxiety disorder (GAD) and MetS in a large study of male US veterans, GAD was said to be positively associated with MetS but depression was not (Carroll et al., 2009). This is

consistent with our study since there was some level of significant association between Mets and GAD. In another cross-sectional study conducted in Thailand among temple members aged between 35- 65 years in several Buddhist Temples (Peltzer & Pengpid, 2018), it was reported that there was no significant association between MDD, GAD and (Peltzer & Pengpid, 2018) MetS. The results contradict findings from this current study where there was an association between MetS and GAD. In another population-based cross-sectional study on MetS and psychiatric disorders among young adults between the ages of 21-31years, it was reported that GAD had the highest association with MetS than the other psychiatric disorders (Moreira et al., 2019). The observed association of MetS and GAD may be due to the effect of stress on the autonomic nervous system activation and stimulation of the endocrine system resulting in the production of hormones that brings about some of the components of MetS.

5.8 Conclusions

This study has shown that, in young Ghanaian adults, the prevalence of MetS was high among the female participants (37.4%) as compared to their male counterparts (18.4%), with an overall prevalence estimated at 27.96%. The study provides novel data that metabolic syndrome is a significant predictor of anxiety and not depression in sub-Saharan Africans. The study again showed that GAD had a significant association with MetS. Furthermore, the study provides data that females had a high prevalence of MetS. The study also indicated or showed an association between all the components of MetS, GAD and obesity. It also provides data that MetS does not have any significant relation to or association with depression. The study also gave data that MetS had no significant relation to depression and gender.

5.9 Limitations of the study

This study had several limitations. First, because the design of the study was cross-sectional, we could not make temporal inferences regarding the directionality of the relations between anxiety and depression symptoms and metabolic components. Also, lifestyle (e.g. exercise, diet), medication usage, and comorbidity were not controlled for in this study. Furthermore, as the participants were recruited from the same community, they were likely to share genetic and environmental factors, which may cause a likelihood of inflated significant findings.

5.10 Recommendations

Because these factors such as lifestyle (e.g. exercise, diet), medication usage, and comorbidity were not controlled, it will be important to examine these effects in future research. Future directions include adding diet and exercise. This can help to reveal the impact each of these factors has on psychological wellbeing and metabolic syndrome components. Larger sample size and more even ratios of females to males would have helped more to generalize the study.

Future studies can also be done by longitudinally, as this can help to determine directionality. Lastly, it would be quite interesting to look at this data set in relation to stress-induced emotional eating and the HPA (hypothalamic-pituitary-adrenal) axis. This is the idea that stress causes an increased desire for high-calorie foods. When comfort food is eaten, it may change signals in the brain, lowering the response to stress (Yau & Potenza, 2013). The HPA axis could be examined in part by adding blood cortisol levels and diet to the model, as well as doing the longitudinal study. Considering the high rate (56.8%) of MetS among the study participants, it is recommended that; intense public education on MetS for Ghanaians is essential if the health of the nation is to improve. The association of MetS with anxiety will

also require the imputation of screening for GAD in the primary care settings and also during general community health screenings.

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